REMARKS

Applicants have amended Claim 14 as discussed below. Applicants have also added a new Claim 27 directed to the compound corresponding to the elected species (i.e., alternative (c) of Claim 18). Applicants maintain that all claims are fully supported by the specification.

Restriction Requirement under 35 U.S.C. 121

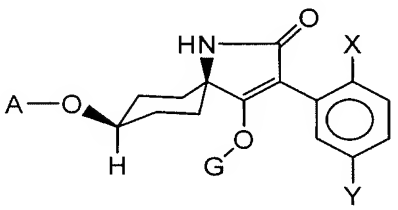
Applicants acknowledge consideration of Group I (i.e., Claims 14-18 and 24) and withdrawal of method Claim 25. For reasons previously presented, Applicants again request rejoinder of method Claim 25 upon finding that the remaining claims are allowable but in any case reserve the right to file one or more divisional applications directed to non-elected subject matter.

With regard to the scope of examination, Applicants note that the Office Action at pages 4-5 specifically address embodiments in which X, Y, and A are alkyl and G is ethoxycarbonyl. Because X and Y are substituents on a phenyl group, for which the electronic effects of varying substituents are reasonably well recognized, because Applicants' examples include representative compounds having both alkyl and halogen substituents, and because the reference cited in the anticipation rejection discussed below discloses compounds in which alkyl and halogen substituents are mentioned, Applicants submit that their current amendments to Claim 14 in this respect (and their retention of the very narrow scope of Claim 18) are reasonable and would not impose an undue burden on examination. Furthermore, because carbonyl groups other than ethoxycarbonyl would readily be understood to be structurally and functionally related to ethoxycarbonyl and to one another, especially when limited as Applicants have done by amendment to Claim 14 (and as narrowly defined in unamended Claim 18) and because the reference cited in the anticipation rejection discussed below itself discloses compounds in which G varies considerably, Applicants submit that their current amendments in this respect (including retention of the "parent acid" when G is hydrogen) are also reasonable and would not impose an undue burden on examination. Applicants therefore request consideration of their claims as amended upon finding that examined embodiments are allowable.

Rejection under 35 U.S.C. 102

Claims 14-18 and 24 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 6,114,374 ("Lieb et al"). Applicants respectfully traverse.

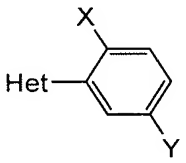
By way of preliminary comment, Applicants first note that their claims are directed to compounds having the particular stereochemistry represented in the formula (I)



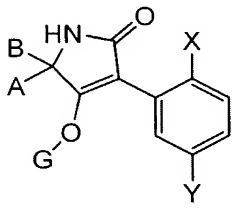
(I)

in which groups X, Y, A, and G are as defined in Claim 14.

Lieb et al discloses compounds of the formula



in which Het represents any of four heterocyclic groups, one such group defining pyrrole compounds represented by the formula (drawn with the same orientation as shown for Applicants' formula (I) for convenience of the Examiner)



in which **X** can be halogen, (halo)alkyl, alkenyl, alkynyl, (halo)alkoxy, cyano, or nitro; **Y** can be hydrogen, amino, halogen, (halo)alkyl, (halo)alkoxy, hydroxyl, cyano, nitro, or one of several optionally substituted (hetero)aromatic groups; **A** and **B** can individually represent alkyl or other substituents or together can represent an optionally substituted carbocycle (including cycloalkyl) or heterocycle; and **G** can be hydrogen or various acyl or acyl-like substituents. E.g., column 1, line 46, though column 3, line 53, as well as column 16, lines 28-34 (A and B together). That is, the substituents disclosed in the reference include groups found in Applicants' claimed invention. In addition to disclosing compounds having the basic formula shown above, Lieb et al states that such compounds can be separated into their isomers by known methods (e.g., column 3, lines 54-65, as well column 8, lines 62-67) but provides no information about how to do so for any of the disclosed compounds (including the pyrrole compounds represented in the formula above). Furthermore,

for compounds in which A and B together form a cycloalkyl ring, Lieb et al discloses synthetic methods for preparing cyclic precursors as "mainly" β-isomers by the Bucherer-Bergs synthesis or as mainly α-isomers by the Strecker synthesis (see column 40, lines 17-49), each of which precursors must then be converted to intermediates that are ring closed to form the final products (e.g., column 40, line 50 et seq). Without further elucidation, the term "mainly" could mean that as little as about 51% of the respective isomers could be present. The Preparation Examples at columns 60 to 67 of the reference describe the preparation of specific pyrrole compounds, along with the tables that provide structural elements and their respective melting points. Although the tables indicate that the various compounds are obtained as the β-isomers, Lieb et al does not provide examples showing the preparation of the corresponding isomeric precursors, much less describe their isomeric purity other than stating that the final products are β-isomers (which, as mentioned above, must be read as being only "mainly" β-isomers).

Regardless of how the reference is interpreted in this respect, a comparison of the melting points of the compounds of Applicants' invention with those disclosed in the reference clearly show that their inventive compounds are not the same as corresponding compounds of the reference. In particular, a 99.6% pure sample of Applicants' compound of Example I-c-1 (i.e., their elected species) has melting point of 142-143°C (see specification at page 87, line 16), whereas Lieb et al teaches that the compound prepared according to its Example I-1-c-4 has a melting point of 128°C (see Lieb et al in the table at bottom of column 64). Based on this difference in physical properties, Applicants' compound is clearly different from the compound prepared according to the reference.

Furthermore, it is well established that stereoisomers can be patentable, even in the face of general suggestion about such isomers. For example, it has long been recognized that "the novelty of an optical isomer is not negated by the prior art disclosure of its racemate" (*In re May and Eddy*, 574 F2d 1082, 197 USPQ 601, 607 (C.C.P.A. 1978), citing *In re Williams*, 36 C.C.P.A. 756, 171 F.2d 319, 80 U.S.P.Q. 150 (1948)), where some claims were rejected but others were deemed patentable. The C.C.P.A. also held that the "totality of the *evidence of record*" supported a finding of patentability over an obviousness rejection. *In re Petrzilka*, 424 F.2d 1102, 165 U.S.P.Q. 327, 328 (C.C.P.A. 1970) (emphasis in original); compare the D.C. Circuit decision *Brenner v Ladd*, 247 F. Supp. 51, 147 U.S.P.Q. 87, 91 (D.C. Cir.

1965). More recently, the C.A.F.C. in *Forest Laboratories v. Ivax Pharmaceuticals*, 84 U.S.P.Q.2d 1099 (Fed. Cir. 2007), upheld the allowability of claims directed to a substantially pure optical isomer in the face of a prior art disclosure of the corresponding racemate and a statement that optical isomers might have improved activity. Although the pharmacology paper discussed in the *Forest Laboratories* decision was not a chemical paper, the conclusion that the failure of the paper to anticipate or suggest the claims then at issue was related to an absence of any disclosure substantially pure isomers or how to obtain such isomers. E.g., *Forest Laboratories* at 1103. See also *Sanofi-Synthelabo v. Apotex*, 550 F.3d 1075, 89 U.S.P.Q.2d 1370, 1379-1380 (Fed. Cir. 2008), in which the C.A.F.C. similarly held that claims for an optical isomer were not anticipated or rendered obvious by prior disclosure of the racemate. Even when rejections have been affirmed, it is clear that the rejections were sustained because unexpected results were absent or not sufficient. E.g., *Brenner v Ladd* at 147 U.S.P.Q. 91 (finding unpatentability of some claims "in the absence of unexpected or unobvious beneficial properties"); see also *In re Adamson and Duffin*, 275 F.2d 952, 125 U.S.P.Q. 233, 235 (C.C.P.A. 1960). Here, Applicants have shown unexpectedly enhanced results consistent with patentability of their claimed invention. In particular, Applicants' specification provides data showing that the inventive compound of their Example I-c-1 is biologically more active than a compound prepared using the method described for the compound of Example I-1-c-4 of the reference as a mixture having cis:trans ratio of about 81:18. See specification at page 90, lines 8-13, as well as the data in Table A at page 93 and Table C at page 97.

Applicants therefore respectfully submit that their claimed invention is not anticipated or even rendered obvious by Lieb et al.

Supplemental Information Disclosure Statement

During the prosecution of Applicants' counterpart Japanese patent application, Applicants became aware of JP 2002/205,984 (copy of English abstract enclosed). Applicants note by way of comment that the disclosed compounds always have an R^1–X– moiety (where X is O or S) attached to the pyrrole ring nitrogen atom, a feature not found in the compounds of Applicants' invention.

In view of the preceding amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

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